

# Synthesis of *cis*-Monolignols

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## Introduction

*cis*-Cinnamic acids have been found in specific plants with important physiological roles in development. *cis*-Coniferyl alcohol also has been isolated from some plants. We are interested in the role of *cis*-monolignols in plant development and the specific characteristics of lignin structure if both *cis*- and *trans*-monolignols are incorporated. The study of synthetic lignins (DHPs) from *cis*-monolignols will aid in understanding the role of *cis*-monolignols in plants. Until now, the major problem confronting the study is that *cis*-monolignols are reported to be unstable and easily isomerised to *trans*-isomers, so the pure *cis*-isomers are hard to synthesize. Here we report a new method to synthesize the *cis*-monolignols in high yield and extremely high purity.

## Methods

The reaction pathway for *cis*-coniferyl alcohol synthesis is shown in Figure 1. *p*-Coumaryl alcohol and sinapyl alcohol can be synthesized similarly.

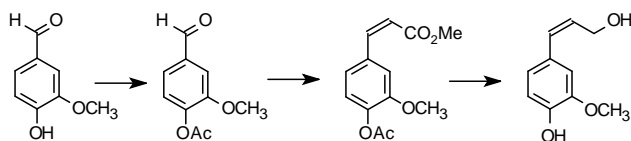


Figure 1. Synthesis of *cis*-coniferyl alcohol.

## Results and Discussion

Traditionally the *cis*-monolignols are synthesized via photo induced isomerization of *trans*-isomers. The major problem of this method is that the

resultant product is a mixture of *cis*- and *trans*-isomers from which separation is difficult. So until now, research of the role of *cis*-monolignols in lignin structure and plant development has utilized the mixture, complicating the results.

*trans*-Ferulate is easily constructed with vanillin and triethylphosphonoacetate via an HWE reaction. The transition state strongly favors the *trans*-configuration. Some reports have shown that the replacement of the ethyl group with trifluoro group will make the *cis*-configuration much more favorable. We figured that the transition state would still favor the *cis*-isomer using vanillin as the substrate. The reaction was indeed successful, resulting in pure *cis*-ferulate in 95% yield. The normal phenol protecting group in this reaction is an ether, but its cleavage under mild acidic conditions resulted in some isomerization. In order to avoid this drawback, acetate was used as a protecting group. The acetyl group need not be cleaved after the formation of ferulate and can be directly reduced in the DIBAL reduction step to afford the coniferyl alcohol. Acetate is not normally used as a protecting group in alkaline conditions, but in this reaction it worked very well. Additionally, the ferulate acetate is much easier to crystallize than the ether-protected ferulate. The final DIBAL reduction afforded *cis*-coniferyl alcohol; it was crystallized from acetone/water or acetone/petroleum ether in 85% yield. The *cis*-sinapyl and *p*-coumaryl alcohols are synthesized analogously with yields of 82% and 81%.